EVALUATION OF A ^{133}Xe VENTILATION TECHNIQUE FOR DIAGNOSIS OF PULMONARY DISORDERS

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Regional perfusion deficits are present in a variety of lung disorders. Determination of the relationship of ventilation to perfusion has been suggested as a means of providing information for differentiating the etiology of such deficits. A marked reduction in perfusion with approximately normal ventilation resulting in high ventilation/perfusion ratios was demonstrated in pulmonary embolism with a multiprobe method of determining ventilation (*1–2*). Comparisons of perfusion scintigrams made with a scintillation camera with those obtained after inhalation of radioxenon has proved valuable for differentiating the perfusion defects of pulmonary emboli from those of other disorders (*3*). Similar scintigraphic comparisons of patients with chronic obstructive pulmonary disease produced a constellation of findings unlike those reported in pulmonary embolization (*4*). Despite other reports of methodology (*5*) for determining this ventilation/perfusion relationship, few clinical correlations have been reported.

The results of studies of a group of patients with a variety of pulmonary disorders having successive perfusion and ventilation scintigrams are the basis of this report. These results expand and modify the previously reported experience.

METHODS

The study group is composed of 42 patients. Each of 33 successive patients with a defect in the perfusion scintigram had a ventilation study performed within 24 hr. In addition, a ventilation study was performed in each of nine patients who had a normal perfusion study.

All scintigrams were made with a Pho/Gamma III scintillation camera. A dual region-of-interest system (*6*) continuously recorded the counting rate from each lung during the ventilation study. Comparison of scintigrams was done by visual inspection. Perfusion scans were made with either ^{131}I-macroaggregated albumin (75–100,000 counts/view) or ^{99m}Tc-albumin microspheres* (200,000 counts/view).

Radioxenon for the ventilation studies was obtained in cylinders. Balloons of capacity approximately equal to the volume calculated to deliver 10 mCi (200–1,000 ml) were filled from the cylinder without tension as needed. Each patient initially breathed oxygen from a 5-liter spirometer. The balloon with the radioxenon was attached to a sidearm near the mouthpiece. Following a maximal exhalation, the sidearm was opened; the patient inhaled maximally and held his breath for the next 10–20 sec while a scintigram was made. Usually 100,000 counts were accumulated, but in patients with severe tachypnea fewer counts were obtained. The patient then quietly rebreathed from the spirometer until equilibrium was achieved as determined by a constant counting rate in each lung field. A scintigram of the equilibrated lungs was made. The patient then breathed room air, and a series of 30-sec-exposure scintigrams was made during washout with an automatic 35-mm camera attached to the oscilloscope of the scintillation camera.

The counts obtained in 2-sec intervals from each lung field from first inspiration to the end of washout were recorded. As rebreathing into the spirometer proceeded, the counting rate rapidly declined to an asymptote. This asymptotic value was subtracted from the preceding values obtained during rebreathing. Semilog plots of these differences yielded curves that could be fitted readily by a single exponential. Direct semilog plots of the falling counting rate from

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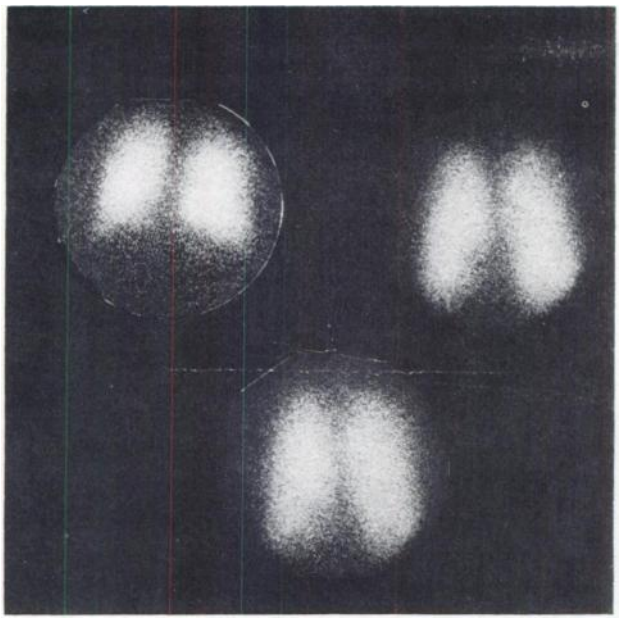

FIG. 1. Normal perfusion and single-breath ventilation study. Patient with acute bronchitis. (In this and subsequent figures upper left is scintigram of perfusion, upper right is single breath ventilation, and lower is equilibrated scintigram. Posterior views are shown with right lung to viewer's right.)

the time of equilibrium through the washout period yielded curves that approximated a biexponential function. However, the half-times of these latter curves could not be determined accurately because of insufficient data collection (~5–8 min of washout) to fit the slow component accurately and the high variability of the data at the low counting rate encountered during washout. Therefore only the half-times of the single exponential obtained from the initial period of rebreathing are considered here.

RESULTS

With the exception of the half-time values, the results are grouped for presentation according to the scintigram findings rather than by diagnostic categories.

Group I. Normal perfusion, normal single-breath xenon distribution. All nine patients with normal perfusion who had ventilation studies requested by the attending physician had normal single-breath and equilibrated ventilation scintigrams. Seven of the patients had acute bronchitis with mild emphysema, one had a left superior sulcus carcinoma, and one was in mild pulmonary edema of heart failure. Figure 1 shows the study of a patient with acute bronchitis. Three of the patients with mild emphysema showed localized retention during washout.

Group II. Perfusion defect with nearly normal single-breath xenon distribution. Eighteen patients had this combination of findings. Fifteen of these had pulmonary emboli. Three patients with these findings had other disorders. Figure 2 shows the study of a patient with pulmonary embolism. Figure 3 is the study of a patient with asthma, and the study shown in Fig. 4 occurred in a patient who had a fibrotic lesion of the right upper lobe. A patient with asthmatic bronchitis had similar findings. The patient with bronchial asthma could be distinguished from the pulmonary embolism patients by prolonged retention in the hypoperfused region during washout which was not seen in the embolism patients. Washout studies of the patients with the fibrotic lesion and

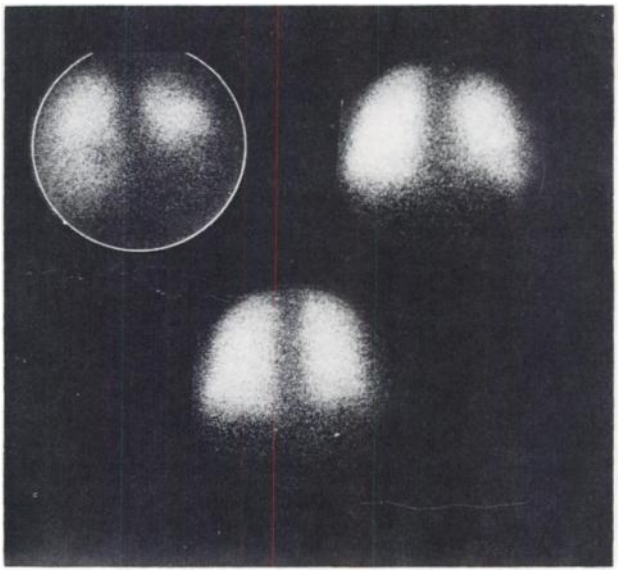

FIG. 2. Pulmonary embolism. Right lower lung field perfusion deficit with minimally diminished single-breath and normal equilibrated ventilation.

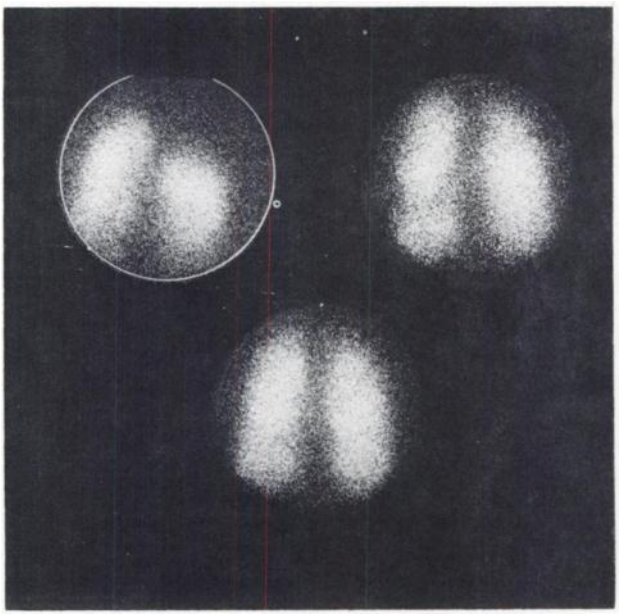

FIG. 3. Asthmatic patient. Right apex is poorly perfused but better ventilated with single breath. In addition, there is small ventilatory defect of left lower lung.

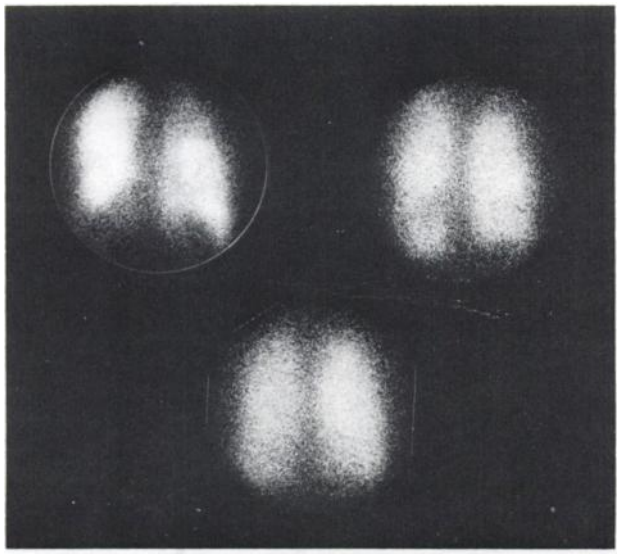

FIG. 4. Right upper lobe fibrosis of undetermined etiology. Right apical perfusion deficit with normal single-breath distribution.

the asthmatic bronchitis were of poor quality, and the ability of this phase of the study to discriminate ventilatory from embolic disease is not answered by these data. Strikingly, all the patients with pulmonary emboli are in this group.

Group III. Corresponding perfusion and single-breath xenon distribution defects. Thirteen patients are in this group. Nine had chronic bronchitis and emphysema, two bronchopneumonia, one noncavitary tuberculosis, and one frank pulmonary edema. Although the ventilation defects correspond anatomically to the perfusion defects, variation is present in the degree of the ventilation deficit compared with the perfusion deficit. More extensive ventilatory deficit is present in two; conversely, lesser ventilatory deficit is present in two. Figure 5 illustrates the findings in a patient of this group. All patients showed filling of the ventilation defect in the equilibrated study. Some degree of regional and/or generalized retention during washout was present in all.

Group IV. Corresponding perfusion and equilibrated ventilation defects. This group is comprised of two patients, one with atelectasis and one with fibrothorax of the right lower lung (Fig. 6). The areas of absent perfusion are almost totally unventilated.

The half-time values of the single exponential curves obtained from first inspiration to equilibration ranged in normal subjects from 4 to 7 sec. Of those 29 patients with studies adequate to calculate the half-time values (Table 1), normal values were obtained in 1 of 5 with acute bronchitis, in 6 of 11 with pulmonary emboli, in 1 of 9 with chronic bronchitis and emphysema, in a patient with a right upper lobe fibrotic lesion, and in a patient with noncavitary tuberculosis with infiltrates.

Three of the five patients with pulmonary embolism and prolonged half-times had, in addition, known chronic obstructive lung disease and were in the care of chest physicians.

DISCUSSION

Availability of radioxenon in a form allowing ready administration by inhalation of measured amounts stimulated these and other recent studies (*3–4*) designed to determine the diagnostic usefulness of comparative ventilation and perfusion scin-

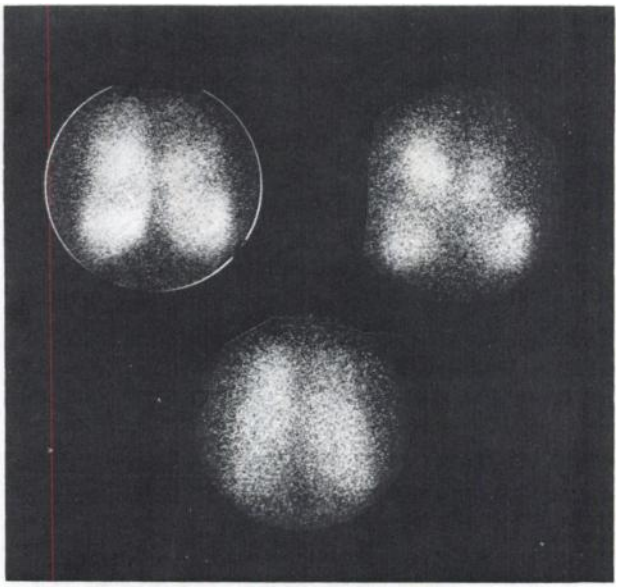

FIG. 5. Chronic bronchitis and emphysema. Corresponding perfusion and single-breath ventilation abnormalities. Normal equilibrated radioxenon distribution.

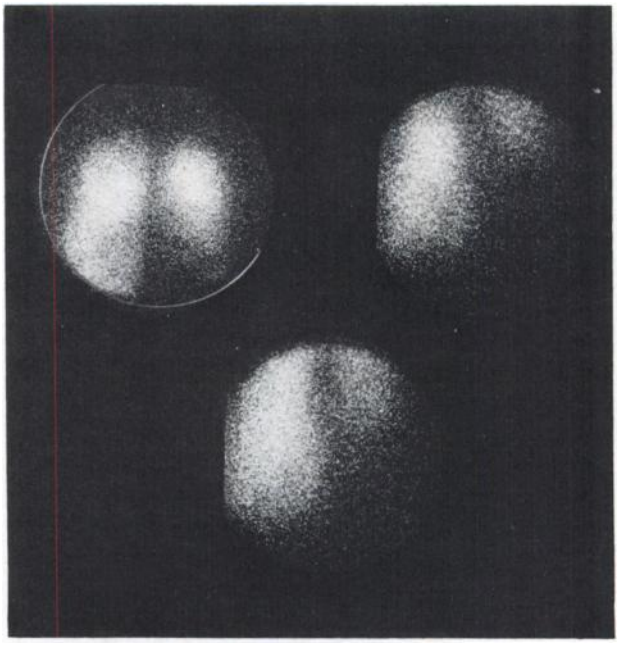

FIG. 6. Right fibrothorax. Corresponding perfusion, single-breath, and equilibrated ventilation defects are present.

TABLE 1. HALF-TIME OF EQUILIBRATION

	Patient	Sex	Age	$T_{1/2}$ (sec)	
Acute bronchitis	KCon	F	39	9.5	
	FF	F	70	11.0	
	KCot	F	49	14.0	
	JK	M	31	6.0	
	GO	M	74	16.0	
Pulmonary embolism	JA	M	77	7.0	
	JeS	M	68	22.0	
	DG	F	65	6.0	
	PI	M	81	24.0	
	JT	M	46	7.0	
	PW	M	66	5.5	
	JoS	M	73	12.0	
	RB	F	65	9.0	
	VB	F	47	5.0	
	MC	F	39	12.0	
	CH	M	54	5.0	
Chronic bronchitis-emphysema	SW	F	67	16.0	
	LH	M	70	12.0	
	BG	F	72	13.0	
	NS	M	53	19.0	
	PC	F	59	18.0	
	HM	M	75	12.0	
	AD	M	54	10.0	
	ER	M	59	7.0	
	HR	M	61	12.0	
Miscellaneous	FP	M	56	5.0	(Tbc)
	JR	M	52	10.0	(Bronchiectasis)
	AH	F	39	19.0	(Asthma)
	MA	M	69	6.0	(RUL fibrosis)

tigrams. Our primary goal was to determine the value of a radioxenon study in patients with perfusion defects rather than the spectrum of ventilatory abnormality. In establishing such studies a particular technique should be maintained until sufficient data accumulates to evaluate the method. Delivering the gas in a single breath was selected *a priori* as likely to distinguish rapidly exchanging regions of the lung from slower ones. With the concentration of radioxenon employed, a vital capacity breath was used of necessity to insure delivery of up to 1,000 ml in one breath. Tidal breathing was used during washout.

Using quite similar techniques, our results confirm those of DeNardo and colleagues that pulmonary embolism is characterized scintigraphically by perfusion defects with normal distribution of a single breath of radioxenon (*3*). The scintigraphic method in turn, confirms the data derived by probe techniques (*1–2*). However, three patients with other lung diseases had the same scan findings. These three patients may represent disorders other than pulmonary embolization that can produce perfusion deficits without major ventilatory impairment. However, at least one of these patients had a ventilatory deficit detectable in washout. Alternatively, lesser ventilation deficits may be unrecognized by the technique of delivering the tracer with a vital capacity breath. Recent development of a system* capable of delivering the needed activity in very small volumes (0.1–1.0 ml) permits the comparison of tidal with vital capacity breaths. In the few such comparisons we have undertaken, the extensiveness of the ventilatory deficit noted with a tidal breath is greater in some patients when compared with a vital capacity breath. So far, we do not have sufficient experience to make a conclusion.

Corresponding areas of perfusion and ventilatory deficit are present in a variety of disorders. In this series, the disorders are characterized by either pulmonary infiltration visible on chest x-ray (bronchopneumonia, noncavitary tuberculosis, pulmonary edema) or chronic pulmonary disease with variable combinations of emphysema and bronchitis. The relative degree and extent of the deficit in the ventilation and perfusion scintigrams were highly variable, about half showing greater perfusion and half greater ventilatory impairment by this technique. No relationship to diagnosis was apparent.

Except in two cases where no ventilation was present in a region (one with atelectasis and one with a fibrothorax) scintigrams obtained after equilibration of the lungs with the spirometer were uninformative. However, equilibration was reached to insure sufficient radioactivity in poorly ventilated portions of lung to obtain clear evidence of retention during washout.

In a group of 40 patients with chronic obstructive pulmonary disease Medina and coworkers (*4*) found eight with no ventilation or perfusion abnormality scintigraphically, eight others with trapping noted in washout as the only abnormality, and six with normal perfusion and abnormal single-breath ventilation and washout. Only 18 of their patients had perfusion deficits, and these all showed single-breath ventilation and washout abnormalities, as did all our patients with this disorder. Our small group of patients with normal perfusion had acute generalized pulmonary disease with one exception, and alone provided the opportunity for finding ventilation defects without perfusion defects. Three washout abnormalities were found with no single-breath maldistribution noted. In the remainder of our patients ventilation was not evaluated unless a perfusion deficit was present.

Washout scintigrams, taken at 30-sec intervals, provided additional diagnostic information in several patients. This phenomenon has been suggested as a more sensitive indicator of ventilatory abnormality than uniformity of single-breath distribution (*4*). Half-times of equilibration also quite sensitively

* New England Nuclear Corp., Boston, Mass.

detected ventilatory abnormality in our series of patients. Prolonged half-times were present in several patients with pulmonary embolization. Several of these patients were elderly with emphysema. This disorder is so common in our population that trapping during washout and long half-times of equilibration are seen frequently in each primary diagnostic category.

SUMMARY

Forty-two patients had perfusion and serial radioxenon ventilation scintigrams. Radioxenon was administered in a single vital capacity breath and scintigrams made of the single-breath distribution, the distribution at equilibrium and serially during washout.

Normal perfusion and single-breath ventilation were present in a small group of patients with acute bronchitis and in single patients with pulmonary carcinoma and mild pulmonary edema. Washout was abnormal in three of these.

A perfusion defect with normal single-breath ventilation was present in each of 15 patients with pulmonary embolism. Three additional patients with asthma, asthmatic bronchitis, and an upper-lobe fibrotic lesion had similar patterns. Trapping during washout in the asthmatic patient was of discriminatory value.

Corresponding perfusion and single-breath ventilation defects were present in patients with pulmonary infiltrates or chronic obstructive disease.

The distribution after equilibration was abnormal only in two patients with completely nonaerating regions of lung.

Segmental trapping during washout and half-times of equilibration curves were sensitive indicators of mild ventilatory difficulty but were of differential diagnostic value only occasionally.

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